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OFFICIAL

DATE: January 9, 2004

TO: Art Unit 1631
MAIL STOP Non-Fee Amendment

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FROM: John D. Goodhue

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COMMENTS: Please file the attached RESPONSE TO RESTRICTION REQUIREMENT:

APPLICANT : MARANAS et al.
SERIAL NO : 10/043,440
FILED : January 10, 2002
TITLE : METHOD AND SYSTEM FOR MODELING
CELLULAR METABOLISM

Grp./A.U. : 1631
Examiner : MORAN, Marjorie A.
Conf. No. : 1336
Docket No. : P05468US1

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RESPONSE TO RESTRICTION REQUIREMENT

Commissioner for Patents
P.O. Box 1450
Mail Stop Non-Fee Amendment
Alexandria, VA 22313-1450

Sir:

In response to the Restriction Requirement dated December 15, 2003, please consider the following remarks on the above-identified application.

CERTIFICATE OF MAILING/TRANSMISSION (37 CFR 1.8(a))

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☒ transmitted by facsimile to the Patent and Trademark Office, Art Unit 1631 at Fax No. (703) 872-9306.

John D. Goodhue
JOHN D. GOODHUE

Amendments To the Claims

Claim 1 (Original): A method for modeling cellular metabolism of an organism, comprising:
constructing a flux balance analysis model;
applying constraints to the flux balance analysis model, the constraints selected from the set
consisting of: qualitative kinetic information constraints, qualitative regulatory
information constraints, and differential DNA microarray experimental data constraints.

Claim 2 (Original): The method of claim 1 wherein the constraints are logic constraints
selected to protect against violation of a kinetic or regulatory barrier.

Claim 3 (Original): The method of claim 1 wherein the constraints are connectivity restraints.

Claim 4 (Original): The method of claim 1 further comprising the step of applying mixed-
integer linear programming to solve for a desired metabolic outcome.

Claim 5 (Original): The method of claim 1 further comprising the step of solving for a desired
metabolic outcome.

Claim 6 (Original): A method for modeling cellular metabolism of an organism that improves
upon a flux balance analysis model, comprising:
constructing the flux balance analysis model; and
applying a plurality of logic constraints to the flux balance analysis model.

Claim 7 (Original): The method of claim 6, further comprising selecting the set of logic constraints to protect against violation a kinetic or regulatory barrier.

Claim 8 (Original): The method of claim 6 wherein the logic constraints are defined by a relationship between changes in reaction fluxes and metabolic concentrations.

Claim 9 (Original): The method of claim 6 wherein the logic constraints are defined by a relationship between reaction fluxes and transcript levels of gene coding.

Claim 10 (Original): The method of claim 6 wherein the logic constraints are represented by binary variables.

Claim 11 (Original): The method of claim 10 wherein a first binary variable represents the presence of a reaction and a second binary variable represents the absence of a reaction.

Claim 12 (Original): The method of claim 6 further comprising applying a computational procedure to identify a minimal set of metabolic reactions.

Claim 13 (Original): The method of claim 12 further comprising selecting a growth rate, and wherein the step of applying a computational procedure is applying a computational procedure to identify the minimal set of metabolic reactions capable of supporting the growth rate.

Claim 14 (Original): The method of claim 6 further comprising the step of applying mixed-integer linear programming to solve for a desired metabolic outcome.

Claim 15 (Original): The method of claim 6 further comprising the step of solving for a desired metabolic outcome.

Claim 16 (Original): The method of claim 15 further comprising engineering a change in an organism based on the desired metabolic outcome.

Claims 17-18 (Cancelled)

Claim 19 (Original): A system for modeling cellular metabolism of an organism, comprising:
a flux balance analysis model;
a plurality of constraints applied to the flux balance analysis model, the constraints selected from the set consisting of: qualitative kinetic information constraints, qualitative regulatory information constraints, and differential DNA microarray experimental data constraints.

REMARKS

The Examiner has restricted this application to one of the following inventions under 35 U.S.C. § 121:

- I. Claims 1-16 and 19, drawn to a method and system for modeling cellular metabolism of an organism.
- II. Claims 17-18, drawn to a method of determining a reduced genome.

The Applicants elect claims 1-16 and 19, drawn to a method and system for modeling cellular metabolism of an organism. Claims 17-18 have been cancelled without prejudice to filing a divisional or continuation application including these claims.

No fees or extensions of time are believed to be due in connection with this amendment; however, consider this a request for any extension inadvertently omitted, and charge any additional fees to Deposit Account No. 26-0084.

Reconsideration and allowance is respectfully requested.

Respectfully submitted,

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